Title: How do migraines affect the brain and our cognitive skills?

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Goal: The research aims to get a clear picture of the association between migraine and cognitive impairment in our brains. Compare Episodic and Chronic Migraines.

Introduction

Migraine is a brain and nervous system disorder whose symptoms almost always include intense headaches. A disabling neurological disorder characterized by multiple phases: premonitory, aura, headache, postdrome, and interictal. You get these headaches repeatedly, in episodes that can last anywhere from 4 to 72 hours. Along with head pain, they include other symptoms like nausea and sensitivity to light. One needs to investigate the phase before the headache starts to understand the generation of attacks. The premonitory phase of migraine represents a well-characterized symptom complex. Its duration, however, is not clearly defined, and there are no biomarkers to help define when this phase starts. In total, the premonitory phase consists of a wide range of symptoms that can appear up to 48 hours prior to the onset of pain in a migraine episode. Premonitory symptoms are not often appreciated by patients but have a significant impact on their quality of life. Since these symptoms represent a first step of a migraine attack, they become instrumental in improving our understanding about critical points in the origin of migraine. Its duration, however, is clearly not defined, and there are no biomarkers that may help to define when this phase starts.

The premonitory phase involves a complex interplay between various cortical and subcortical brain regions, including the hypothalamus and brainstem nuclei that modulate nociceptive signaling. The headache phase involves the activation of the trigeminovascular system, a pathway that is well characterized. In one-third of patients, an aura phase may occur during some attacks and likely correlates with a cortical spreading depression-like event; a slowly propagating wave of neuronal and glial cell depolarization and hyperpolarization. Spontaneous oscillations of complex networks involving the hypothalamus, brainstem, and dopaminergic networks lead to changes in activity in certain subcortical and brainstem areas, thus changing susceptibility thresholds and not only starting but also terminating headache attacks.

People with migraine frequently report cognitive difficulties, impacting their daily lives. Research suggests that abnormal brain network connectivity may underlie these cognitive impairments. The findings of resting-state functional MRI studies have suggested that abnormal functional integration between interconnected cortical networks characterizes the brain of patients with migraine.

This research addresses the pathophysiology of migraines and how it affects the brain and cognitive functions. It will create a summary of findings on the chosen topic.

Methods

Quantitative type of research methods were chosen, so the problem can be observed more accurately.

By using a quantitative approach, it is possible to collect statistical data and analyze them from a mathematical point of view. It will provide us with the exact data that is crucial to the research because it will help us understand how many people suffer from the effects of chronic migraines, while also encouraging us to get better treatment for this issue. The collection of data can be done by using previous research papers, questionaries and etc. For this paper, we used two clinical studies that have expired both Chronic migraine, Episodic migraine and Subjective Cognitive Decline, and had over 200 patients to gather the information and data from.

Results

In this section of the paper, we will present the results of our analysis, underlining the effects of migraine on different cognitive domains.

There were several clinical studies that were analyzed and used as a primary piece of data.

One of which focuses on investigating the cognitive profile in patients with chronic migraine (CM) compared to those with low-frequency episodic migraine (EM). Chronic migraine is a disabling neurological disorder that imposes a considerable burden on individual and socioeconomic outcomes. Chronic migraine is defined as headaches occurring on at least 15 days per month with at least eight of these fulfilling the criteria for migraine. Chronic migraine typically evolves from episodic migraine as a result of increasing attack frequency and/or several other risk factors that have been implicated with migraine chronification. They had 144 patients with CM and 44 age-matched patients with low-frequency EM.
The researchers used standardized tools such as the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE) to screen for cognitive impairment, focusing on domains like memory, attention, language, and executive functions. To assess specific cognitive deficits, tests like the Stroop Test, which measures cognitive flexibility and processing speed, and the Trail Making Test (TMT), which evaluates attention, visual processing, and executive functioning, were administered. Additionally, the study incorporated the Rey-Osterrieth Complex Figure

Test (ROCF) to assess visuospatial abilities and visual memory. Self-reported questionnaires such as the Migraine Disability Assessment (MIDAS) and the Headache Impact Test (HIT-6) were also utilized to measure the frequency and severity of migraines, as well as their impact on daily activities and overall quality of life.[1]

	EM	CM	p-value
n	44	144	-
Gender, female/male	40/4	132/12	0.5
Age, years	37.0 (30, 42)	42.5 (31, 50)	0.06
Education, years	14.5 (10, 15)	14.0 (12, 15)	0.3
Headache frequency, days/month	3.0 (2, 4)	20.0 (15, 23.5)	0.00
Frequency of analgesic intake, days/month	2.0 (2, 4)	17.0 (10, 22)	0.00
Headache history, years	17.5 (13, 27)	22.5 (15, 32)	0.25
Chronic headache history, years	-	3,0 (1, 5)	-
Age of CM onset, years	-	36 (25, 46)	-
MOH, %	-	67.4	-
Anxiety, HADS points	5.0 (4, 6)	9.0 (6, 12)	0.00
Depression, HADS points	4.5 (2, 8)	6.0 (4, 9)	0.002

EM: episodic migraine; CM: chronic migraine; HADS: Hospital Anxiety and Depression Scale; MOH: medication overuse headache. Results are presented as median (Q1, Q3).

Figure 2. A summary of demographic and clinical characteristics (Nina Latysheva et al., 2020)

Hospital Anxiety and Depression Scale (HADS) defines depression/anxiety as absent at 0–7 points, subclinical at 8–10 points, and clinical at over 11 points. The Digit symbol substitution test (DSST) is a paper-and-pencil cognitive test presented on a single sheet of paper, that requires a subject to match symbols to numbers according to a key located on the top of the page. The subject copies the symbol into spaces below a row of numbers. The number of correct symbols within 90 seconds constitutes the score. The DSST is a valid and sensitive measure of cognitive dysfunction impacted by many domains. Performance on the DSST correlates with real-world functional outcomes. The PDQ-20 is a self-report tool designed to measure cognitive dysfunction. It includes 20 questions that assess various aspects of cognitive functioning, such as attention and concentration, retrospective memory, prospective memory, and planning and organization. The MoCA total score ranges

from 0 (worst performance) to 30 (best performance), with 26 points taken as the cutoff value for mild cognitive impairment.

	EM	CM	p-value
PDQ-20, points	19.0 (12, 27)	22.0 (16, 34)	0.04
PDQ-20, attention/ concentration	8.0 (5, 11)	7.0 (5, 11)	0.98
PDQ-20, retrospective memory	4.0 (1, 8)	4.5 (3, 7)	0.17
PDQ-20, prospective memory	4.0 (3, 7)	4.5 (2.5, 7)	0.94
PDQ-20, planning/ organization	6.0 (3, 9)	6.0 (2.5, 8)	0.21
DSST, correct symbols	49.5 (46, 55)	42.0 (36, 49)	0.000
RAVLT total learning, words	35.0 (31, 41)	31.0 (26, 37)	0.001
RAVLT leaning rate	0.0 (-1, 1)	0.0 (-2, 1)	0.26
RAVLT delayed recall	1.0 (0, 1)	1.0 (0, 2)	0.18
MoCA, points	28.0±3.0	27.5 (26.5, 29)	0.08

EM: episodic migraine; CM: chronic migraine; PDQ-20: Perceived Deficits Questionnaire; DSST: Digit Symbol Substitution Test; RAVLT: Rey Auditory Verbal Learning Test; MoCA: Montreal Cognitive Assessment. Results are presented as median (Q1, Q3).

Figure 3. Cognitive profile of the chronic migraine and episodic migraine populations (Nina Latysheva et al., 2020)

The MoCA results were lower in CM subjects when compared to EM ones, but within the normal range in both groups. Nonetheless, 18% of CM subjects and 6.8% of controls scored lower than the cut-off point for mild cognitive impairment even when pain-free or almost pain-free. CM patients demonstrated the most striking impairment in memory/delayed recall (65.3%), attention (46.5%), abstraction (30.6%), and language (27.1%). No differences in cognitive performance were observed between patients with and without Medication Overuse Headache (MOH). Pain intensity at the time of testing did not correlate with cognitive performance. CM patients had a higher level of depression and anxiety when compared to EM patients. However, because subjects with clinically relevant depression/anxiety were excluded from the study, both of the groups demonstrated HADS-defined absence of depression. Anxiety reached subclinical levels in the CM population. Compared to EM, CM subjects demonstrated higher subjective cognitive impairment as measured by the PDQ-20. CM subjects had a significantly lower Digit Symbol Substitution Test(DSST) performance. Moreover, 28.5% of patients with CM and only 13.6% of patients in the control group had a DSST score in the lower quartile range. In CM subjects the Rey Auditory Verbal Learning Test(RAVLT) total learning score was also

significantly lower when compared to low-frequency EM controls. Patients with CM had 4 times higher odds of achieving a RAVLT total learning score in the lower quartile range when compared to the EM cohort. Patients with chronic migraines show significant impairments in various cognitive areas, such as memory and attention, even during their least painful moments or when they are not experiencing pain at all. This cognitive decline is persistent and does not fluctuate with migraine episodes. Chronic pain, along with education level, is a more reliable predictor of cognitive decline in these individuals than clinical factors or depression. The cognitive issues in chronic migraine patients may be linked to central sensitization (CS) and maladaptive changes in the brain, particularly in regions associated with pain perception, pain inhibition, and cognitive function.

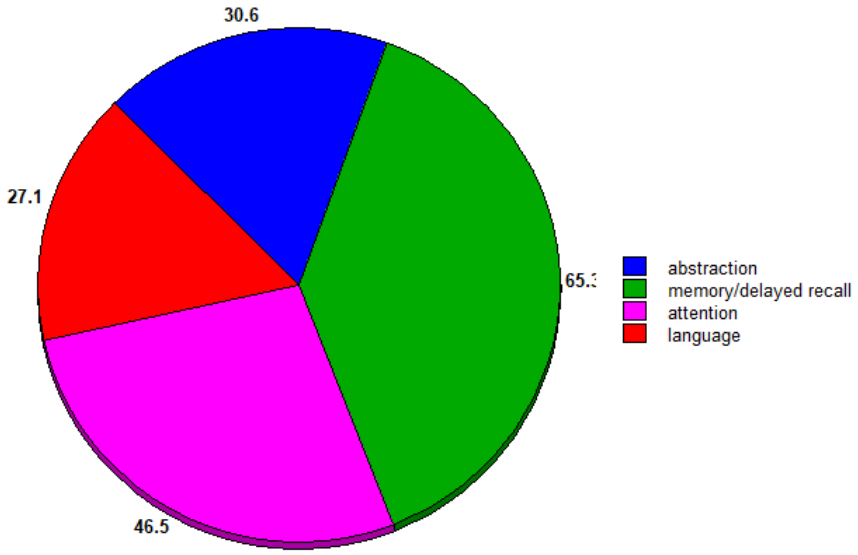

Figure 4. Cognitive Impairment in CM Patients (Nina Latysheva et al., 2020)

The next study was conducted to investigate the presence and frequency of Subjective Cognitive Decline (SCD) in migraine patients and to analyze its association with clinical features, including headache impact, anxiety, depression, and sleep quality. Subjective cognitive decline (SCD), often called "subjective memory impairment" in earlier research, describes when a person feels their cognitive function is worsening, even though cognitive tests don't show any actual impairment. The study was based on a retrospective review of headache registry records from patients who visited the Hallym University Dongtan Sacred Heart Hospital between January and November 2016. Participants included 188 migraine patients who completed cognitive testing and various questionnaires. Cognitive function was assessed using the Korean-Mini Mental State Examination (K-MMSE) and the Korean-Montreal Cognitive Assessment (K-MoCA). SCD was evaluated using a 24-item SCD questionnaire (SCD-Q), and other assessments included the Generalized Anxiety Disorder-7 (GAD-7), the Patient Health Questionnaire-9

(PHQ-9), and the Pittsburgh Sleep Quality Index (PSQI). Data analysis involved t-tests, chi-square tests, correlation analyses, and multivariate logistic regression.

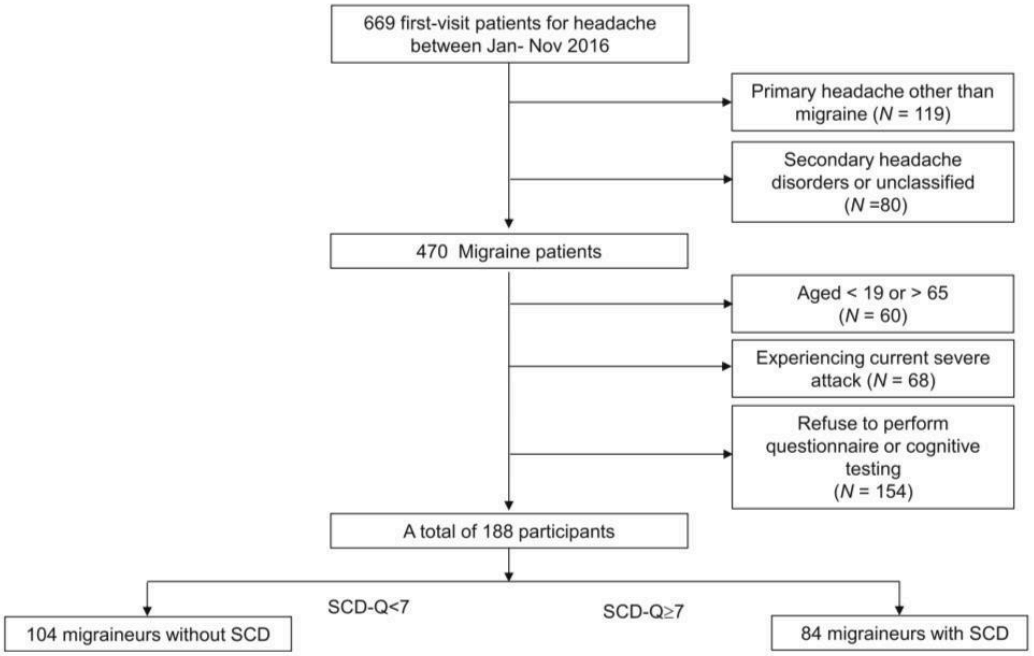

Figure 5. Sample selection diagram (Sun Hwa Lee et al., 2017)

The mean SCD-Q score was 6.5 (SD = 5.5), with 84 patients (44.7%) scoring higher than 7. Thus, 44.7% of participants were diagnosed with SCD in this study. Among the 188 participants, 106 (56.4%) scored higher than the cutoff on the GAD-7, 98 (52.1%) scored higher than the cutoff on the PHQ-9, and 154 (81.9%) scored higher than the cutoff on the PSQI. An independent-sample t-test and Pearson's Chi-square test did not reveal differences between groups in terms of age, sex, migraine type, pain duration, and medication. Additionally, participants rated their average pain intensity using a Visual Analogue Scale (VAS). The impact of headaches was assessed with the Headache Impact Test-6 (HIT-6), which consists of six questions measuring the burden of headaches. These questions covered pain, social functioning, role functioning, vitality, cognitive functioning, and psychological distress. Each question was scored on a five-point scale, with options ranging from 6 (never) to 13 (always). The total score could range from 36 to 78, with higher scores indicating a greater impact.[2]

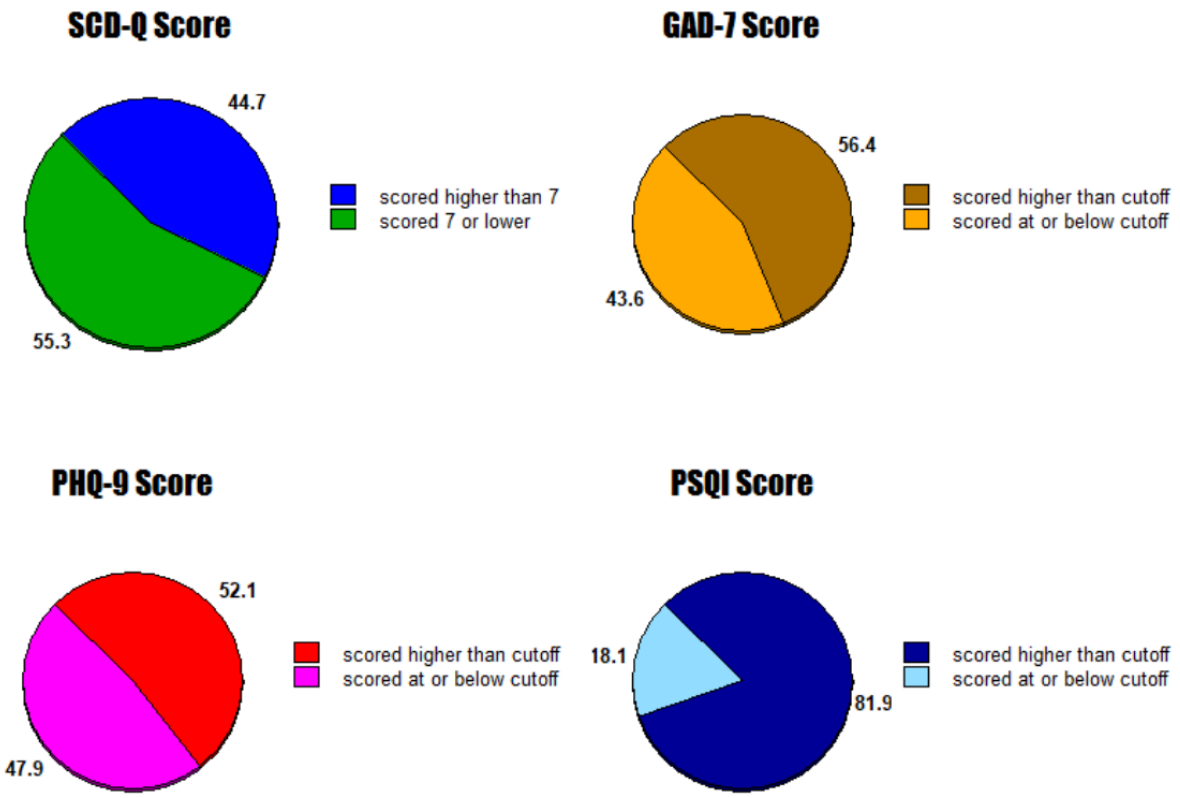

Figure 6. The percentage of participants who scored higher than the cutoff versus those who did not for the SCD-Q, GAD-7, PHQ-9, and PSQI scales. (Sun Hwa Lee et al., 2017)

SCD seems relatively common in adult migraineurs in terms of both gender and migraine subtype. Migraineurs with SCD reported severe pain and the impact of headaches, were more depressed, and anxious, and perceived poorer sleep quality, and shorter sleep duration during weekdays than those without SCD. Depression and shorter sleep duration were significantly associated with the presence of SCD in migraineurs after adjusting other variables.

Discussion

We have investigated two clinical studies that give insights into the cognitive and psychological effects of chronic migraine and the presence of subjective cognitive decline in patients with migraine. Combining qualitative and quantitative techniques has allowed us to derive a comprehensive understanding of how chronic migraines can influence cognitive functions and mental well-being.

In the first study, we note that there are substantial cognitive deficits associated with chronic migraine. Even at times when patients were pain-free or had minimal pain, the test results on standardized neuropsychological tests of memory, attention,

language, and executive functions, like the MoCA, DSST, and RAVLT, remained very low for CM. That could mean that cognitive impairment in patients with CM is more persistent and less dependent on the acute effects of a migraine attack. This would be further supported by a lack of correlation between pain intensity at the time of testing and cognitive performance.

One possible explanation for these results would be the role of central sensitization and maladaptive changes in the brain. These regions of the brain are affected by CS, which is known to influence pain perception, inhibition, and cognitive functions. Therefore, changes induced by CS will be chronic and generalized, hence contributing to cognitive decline. Besides this, according to our research, chronic pain and educational level emerge to become more reliable predictors for predicting cognitive decline in patients with CM than clinical factors or depression, showing that the impact of chronic migraine on cognitive function is grave and complex.

The second study evaluates the prevalence and clinical implications of SCD in subjects affected by migraine. Almost half of the participants, 44.7 %, were diagnosed with SCD—a condition in which people feel they are performing less well cognitively, although their performance on cognitive tests turns out to be within the normal range. The high prevalence of SCD in migraineurs, independent of subtype, underlines that management should consider not only the physical but also the important cognitive and psychological burdens of the migraines.

Moreover, it was found that, compared with migraineurs without SCD, patients with SCD had more severe headaches, higher levels of depression and anxiety, and poorer sleep quality. The findings therefore point to a close association between psychological distress and sleep disturbance in SCD among people with migraine. Notably, after adjustment, the association of SCD remained with both depression and shorter sleep duration, further highlighting the interrelatedness of cognitive, emotional, and sleep-related difficulties in this population.

The results of the study have major implications for clinical practice. Preliminary conclusions that arise from these findings point out the need for health professionals to consider cognitive and psychological aspects of chronic migraine in management. Attention to these may occur with a multidisciplinary approach including neuropsychological assessments, psychological support, and different interventions to enhance the quality of sleep.

Future research should aim to clarify the mechanisms of cognitive decline in patients with CM, mainly central sensitization and brain plasticity. Longitudinal investigations could also involve the long-term effects of chronic migraine on cognitive functioning and possible protective factors. Moreover, the highly prevalent SCD in patients with migraine requires more awareness and screening for cognitive concerns in this population. Such may facilitate early identification and intervention that may help reduce the burden of migraines on cognitive health and overall quality of life. Our study has confirmed that chronic migraine has important implications for cognitive functioning, mental health, and everyday life. By recognizing and acting on these

difficulties, we can gain better management and outcomes in the lives of people with this greatly debilitating condition.

Conclusion

In summary, the performance of CM patients is severely impaired in several cognitive domains, including memory and attention, at their mildest pain and when pain-free. The cognitive deficit is sustained and unrelated to exacerbations of migraine. Chronic pain (and level of education) rather than clinical parameters or depression are independent predictors of cognitive decline in CM subjects. Cognitive impairment in CM may be caused by CS and maladaptive neuroplasticity in the brain areas responsible for nociception, antinociception and cognition. Findings establish the role for timely preventive therapy of EM. The DSST and MoCA are feasible, simple and widely available tools for the examination of time-intensive cognitive performance among migraineurs. Moreover, larger samples are required for further studies on the alteration of cognitive performance through the course of the disease and after treatment.

Moreover, it has been demonstrated that SCD is common in subjects with migraine, particularly those who experience severe headache pain and poor sleep quality. Moreover, this occurs in conjunction with higher levels of depression and anxiety, which may mean that psychological factors and sleep disturbances are major modulators for perceived cognitive decline. The findings underline how early preventive treatment of migraine might help avoid chronic pain, central sensitization, and sustained impairment in cognition.

References

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